SUDDEN INFANT DEATH SYNDROME

Background

Unexplained sudden infant deaths were documented as long as 150 years ago. Prior to 1940, these deaths were often attributed to the mother's "overlying" the infant during sleep. After 1940, when fewer infants slept in bed with their mothers, other possible factors began to be examined. (Beal, 1989)

Today, "Sudden Infant Death Syndrome" (SIDS) is the number one cause of death for infants between the first week of life and one year of age. (Pope, 1983) According to the World Health Organization, a number of European nations have reported a SIDS incidence rate of less than one death per 1,000 livebirths. For instance, Hungary has a SIDS incidence rate of .326 per 1,000 livebirths (1990); Poland has a SIDS incidence rate of .007 per 1,000 livebirths (1990); Bulgaria has a SIDS incidence rate of .08 per 1,000 livebirths (1989); and Czechoslovakia has a SIDS incidence rate of .269 per 1,000 livebirths (1988). (WHO, 1991; WHO 1990; WHO 1989) The incidence of SIDS in the United States ranges between one and three deaths per 1,000 livebirths. (Buck, 1990) The peak age for death among SIDS victims is 12 weeks of age. However, some investigators have reported an age distribution with two peaks (at 8-9 and 13-15 weeks). (Little, 1990)

In 1969, SIDS was defined as "the sudden death of any infant or young child, unexpected by history and in which a thorough postmortem examination fails to demonstrate an adequate cause of death." (Little, 1990) Some researchers began to worry that the use of such a broad definition was allowing the diagnosis to be misused, resulting in the true cause of death being missed or allowing malpractice to be covered up. In response to these concerns, the U.S. National Institutes of Health met in June of 1989 to revise the definition of SIDS. The new definition is as follows:

> The sudden death of an infant under 1 year of age which remains unexplained after a complete postmortem examination, including an investigation of the death scene and a review of the case history. Cases failing to meet the standards of this definition, including those without postmortem examinations, should not be diagnosed as SIDS. Cases that are autopsied and carefully investigated but which remain unresolved may be designated as undetermined, unexplained, or the like. (Zylke, 1989)

Another author wrote:

> Sudden Infant Death Syndrome (SIDS), crib death, or cot death, as it is often called, is the unexpected and often unexplained death of an infant, usually under six months of age. The infant is put to bed in apparently good health or with a mild upper respiratory infection; there is no suspicion of anything abnormal. The infant is of an age (2 months to 6 months) to sleep through the night and, as a result, is not discovered until the next morning.

> There appears to be no warning, no struggle, and no outcry of pain. (Pope, 1983)

The official World Health Organization definition of SIDS is "the sudden and unexpected death of an apparently healthy infant between the ages of two weeks to six months." (Puckett, 1986) Because the majority of Eastern European countries are WHO members, it is fair to assume that the WHO definition of SIDS is accepted in these countries.

As John L. Emery, Emeritus Professor of Pediatric Pathology at the University of Sheffield, observed, very little is actually known about this condition. In fact, many researchers are uncertain as to whether there is actually a single type of infant death known as SIDS or whether it is a collective diagnosis that is assigned to many different types of unexplained infant deaths. (Emery, 1989) Emery wrote:

> Questions are now beginning to be asked, including: Is there such an entity as the sudden infant death syndrome or is it a convenient diagnostic dustbin?

The possibility that SIDS is a "subset of unclassifiable postneonatal deaths," rather than a single entity, has apparently been suggested for a long time. (Little, 1990) One author stated:

> There is a growing conviction among research investigators that the sudden infant death syndrome is not one phenomenon but probably a number of basic mechanisms. (Pope, 1983)

Physiological Mechanisms: Theories

Many theories have been presented regarding the possible physiological mechanism(s) which may lead to the deaths of these infants. However, no theory has yet been identified as the correct one. Victims of sudden infant death syndrome do, however, appear to have a higher frequency of several physiological characteristics than infants dying of other causes. These characteristics include evidence of brain-stem gliosis [an excess of fibrous tissue in the brain-stem region], retention of brown fat around the kidneys, and hepatic erythropoiesis [production of red blood cells in the liver]. (Zielke, 1989) Several authors have also reported an increased immune response in the gastrointestinal and respiratory tracts of SIDS victims. Another author wrote:

> Mechanisms for sudden unexpected infant deaths remain unproven but the possibilities include cardiac arrhythmias, hypoglycemia [low blood sugar], prolonged apnoea [cessation of breathing] from central respiratory control failure, seizure-induced apnoea, prolonged airway obstruction and alveolar atelectasis [incomplete expansion of the alveoli in the lung]. (Southall, 1988)

The author concluded that "there is at present no confirmed physiological predictor of SIDS."

It has also been debated for a long time whether these infants may be dying of subtle infectious respiratory diseases. Some investigators have reported finding evidence of respiratory syncytial virus infection in a small number of SIDS victims. Other researchers have reported finding no evidence of respiratory infection in infants who died of SIDS.

Epidemiology of SIDS

Epidemiological studies have reported a wide range of different factors that are reportedly associated with an increased risk of SIDS. These factors include (but are not limited to) the prone sleeping position, hyperthermia, low birthweight, multiple gestation, low socioeconomic status, maternal substance abuse, microbial factors (bedding), bottlefeeding, lack of prenatal care, timing of prenatal care, maternal smoking, pregnancy complications, prematurity, gender, race, maternal education, month of birth, method of birth, parity [number of births], age of mother, marital status of parents, crowded living conditions, room slept in (own vs. shared), social environment, prenatal development, DPT immunization, ventilation of room, low Apgar scores [a numerical expression of the condition of a newborn infant, usually determined

at 60 seconds after birth, being the sum of points gained on assessment of the heart rate, respiratory effort, muscle tone, reflex irritability, and color), duration of second stage of labor, gestational length, day of the week, and the employment status of the father. However, as one author wrote:

> Epidemiologists, recognizing the uncertainty involved in the diagnosis of SIDS and hence what they count as SIDS, have had to accept the fact that their data lack precision and thus must be interpreted circumspectly. (Peterson, 1988)

Another group of authors wrote:

> In summary, epidemiologic studies have shown that except for the age at which SIDS occurs, no other factor is characteristic enough of the condition to help predict future victims. Instead, we can only recognize certain clinical and socioeconomic characteristics that, although not specific for SIDS victims, appear to carry a higher risk for this fatal outcome. Although the mechanisms for death are still unknown, there is apparently no genetic basis for SIDS and no cause-and-effect relationship between any particular risk factor and SIDS. (Goyco and Beckerman, 1990)

Epidemiologists have attempted, however, to define the profile of the "typical" SIDS infant. One group reported:

> A "disproportionate" number of mothers of SIDS victims are typically multiparous [birth mothers of more than one child], non-white, poor,

> smokers of lower socioeconomic status, who receive late or no prenatal care in spite of a high frequency of pregnancy problems and deliver a small pre-term infant which is then raised in marginal circumstance until its demise.

However, they also conceded that "these factors alone or in combination fail to account for the majority of SIDS occurrences." (Little, 1990) Similarly, Goyco and Beckerman (1990) wrote:

> A profile of SIDS victims characterizes them as previously healthy babies, usually 2 to 4 months of age, possibly with a history of low birth weight and perinatal complications, who have had a viral infection within the previous 2 weeks and die suddenly and unexpectedly while asleep. Their mothers are likely to be young, poor, uneducated, and in most cases cigarette smokers. However, these characteristics of SIDS infants and their mothers appear to be nonspecific and to carry a poor predictive value, because the majority of SIDS victims do not fit this profile and the vast majority of infants who do will not die of SIDS.

While many theories have been proposed regarding the physiological mechanisms and risk factors for these deaths, we still do not know what causes SIDS. According to several research groups, although there are hundreds of published papers on SIDS, its cause or causes remain unknown. (Kraus, 1989; Pope, 1983; Milner, 1989)

As a 1989 article in JAMA observed:

A syndrome of apparently healthy infants dying suddenly and inexplicably was described almost a century ago and has been the subject of systematic study for more than 40 years. But understanding of crucial aspects of sudden infant death syndrome (SIDS) -- what causes it, what infants are at risk, and how to prevent it -- is still limited. (Zylke, 1989)

Smith (1991) wrote:

Given the absence of positive evidence indicating the cause of death and faced only with an infant that is suddenly dead, can we really state with confidence that we know of what the infant died? Who are we protecting? Who are we trying to help? More to the point, who are we kidding?

Goyco and Beckerman (1990) wrote:

SIDS remains a threat to the infant population, and for the most part a mystery to the rest of us.

Environmental Tobacco Smoke

There are six epidemiological studies which have reported associations between parental smoking, as an index of exposure to environmental tobacco smoke, and the incidence of sudden infant death syndrome. The first study to report such an association was Steele and Langworth (1966). This study reported that children of smoking mothers were 2.1-3.6 times as likely to die of SIDS as

were children of nonsmoking mothers. Since 1966, several other authors have reported statistically significantly elevated risks of SIDS associated with exposure to parental (particularly maternal) smoking. (Bergman and Wiesner (1976); Lewak et al. (1979); Malloy et al. (1988); Haglund and Cnattingius (1990); Mitchell et al. (1991))

The major criticism of these studies is that they present no actual exposure data for the SIDS infants. Instead, exposure is based on questionnaire information that is usually obtained from parents. There is no quantitative exposure data in these studies to accurately estimate a SIDS infant's actual amount of exposure to ETS. Without such exposure data, it is impossible to accurately examine the potential relationship between exposure to ETS and the incidence of SIDS.

A second problem with these studies is that even though some of the studies control for several potential confounding factors, other studies control for none or very few of the factors. It has been reported that maternal smoking is associated with such factors as low socioeconomic status, dietary patterns, maternal education, maternal age, etc. Because these other factors have also been reported to be associated with an increased incidence of SIDS, it is critical that they are adequately controlled for in any study which purports to examine the potential relationship

between maternal smoking and the incidence of SIDS. Unfortunately, this is most often not the case.

Finally, it must again be stressed that a physiological mechanism for SIDS has not been determined. It seems to be premature to attempt to implicate isolated factors as being causally related to SIDS when, in actuality, we do not even know what SIDS is.

ecific Claims Regarding Maternal Smoking

aim: **Maternal smoking, both during pregnancy and after birth, may increase the risk of an infant dying of SIDS.**

esponse: Theories continue to be proposed regarding the mechanism involved in sudden unexplained infant deaths; however, the cause of SIDS remains unknown. Therefore, no one is certain about what a SIDS death actually consists of physiologically, and, as a result, it is extremely difficult to isolate any one factor as a possible cause.

Several authors have reported that maternal smoking is one of the factors that often appear on a SIDS infant's profile. However, these authors have conceded that maternal smoking carries a poor predictive value for SIDS and that "the majority of SIDS victims do not fit this profile and the vast majority of infants who do will not die of SIDS."

In a letter to Mr. Robert Flaak, the Assistant Staff Director of the Science Advisory Board Staff Office of the United States Environmental Protection Agency, Professor Milan Samanek, M.D., outlined several

interesting points regarding the claimed association between maternal smoking and SIDS. This letter was in response to the United States Environmental Protection Agency's Revised Draft Risk Assessment on ETS (May 1992), which claims that maternal smoking (during pregnancy and after birth) may be associated with an increased incidence of SIDS. Dr. Samanek first pointed out that "there is an increasing incidence of SIDS in developed countries whereas these countries have a declining rate of smoking." In addition, he stated that "there are regional trends in the incidence of SIDS within a community where the smoking rate is relatively constant." He cited Kahn (1988) as concluding that "[t]he effect of cigarette smoke breathed in by babies has been mentioned but never proven."

Dr. Samanek asserted that an informal review of the literature on SIDS revealed 71 factors unconnected with smoking that may be associated with SIDS. Dr. Samanek stated that the Cnattingius (1990) study cited by the EPA claims a differential effect of maternal smoking on "early" and "late" SIDS. Dr. Samanek suggested that "if this is a passive smoking effect, there should be no difference between these groups; however, if the

relationship is with pre-natal smoking, why are there no cases of SIDS in the first week of life?"

Finally, Dr. Samanek reported that the epidemiological studies of the possible association between maternal smoking and SIDS do not report actual exposure data for SIDS victims. Instead, the studies rely solely upon questionnaire reports of maternal smoking habits. Dr. Samanek stated that "in my opinion, it is impossible to discuss associations with passive smoking and any disease or dose-response relationships without an exposure measurement."

Claim: The United States Environmental Protection Agency's Risk Assessment on ETS concluded that maternal smoking is associated with an increased incidence of SIDS.

Response: While the authors of the Draft Risk Assessment claimed an association between maternal smoking and an increased risk of SIDS, the Scientific Advisory Board panel members suggested that the authors could mention SIDS, but strongly recommended against including it in Chapter 8 on actual risk assessment. (Unofficial Transcripts, 1992) Several of the SAB members felt uncomfortable with the discussion of SIDS because of the general lack of knowledge about the condition. The Risk Assessment presented no original data but only reviewed some of the literature available on SIDS. The studies that the Risk Assessment relied on reported no actual exposure data for the SIDS infants and relied instead upon questionnaire information regarding maternal smoking habits. The EPA Risk Assessment fails to provide a comprehensive review of the scientific literature available on SIDS.

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The Report of the Royal College of Physicians entitled "Smoking and the Young" claims that there is a relationship between maternal smoking and sudden infant death syndrome.

The authors of this Report present no original data but review a select sample of the available literature on SIDS. Although there are over 100 published studies available on SIDS, the Report discusses only three or four studies. The Report fails to discuss the enormous body of literature which suggests that, because of the unknowns involved in SIDS, it is virtually impossible to implicate a single factor as being causally associated with SIDS. Once again, actual exposure data for SIDS infants are not provided in the epidemiological studies cited by the Royal College of Physicians in the Report.

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